CAN DRUG SENSITIVITY OF *LACTOBACILLUS RHAMNOSUS* TO NOVEL DRUGS BE EXTRAPOLATED WITHIN SPECIES?

Piotr Kochan, Agata Pietrzyk, Artur Drzewiecki, Małgorzata Bulanda

International Scientific Conference on Probiotics and Prebiotics – IPC2017, 20-22 June 2017, Budapest, Hungary

INTRODUCTION

As per the latest guidelines on probiotics contained in food or dietary supplements, strains must be selected from a "safe" species with enough evidence confirming the health benefits on the host. According to those latest recommendations, some data may possibly be extrapolated within the given bacterial species contained in the product, especially when it comes to taxonomy or functional comparisons. Such extrapolations, although financially sound, could be dangerous and open a field for assumptions or generalisations. We aimed to see whether drug sensitivity data within the *Lactobacillus rhamnosus* species is comparable for each of the 5 tested drugs, and whether extrapolation is acceptable or even appropriate, thus putting these recommendations in a new light and opening them up for discussion [1].

MATERIAL AND METHODS

The *Lactobacillus rhamnosus* strains, contained in various probiotic preparations, were purchased commercially, exactly as available to the public. After gaining some previous experience regarding lactobacilli and drug sensitivity testing, including problems with zones of inhibition and resistant vs. sensitive breakpoints (Kochan et al. Antimicrobial resistance profiles of selected Polish probiotics, IPC 2010, Kosice, Slovak Republic)[2], we decided it's best to evaluate them using Etests. The following strains, were tested for drug sensitivity: *L. rhamnosus* GG, *L. rhamnosus* PEN, *L. rhamnosus* E/N, *L. rhamnosus* OXY and *L. rhamnosus* KL53A. We selected relatively novel drugs to be used in this study, namely: ceftaroline, ceftobiprole, doripenem, daptomycin and tigecycline. Tests were done in triplicates, to determine the minimal inhibitory concentration (MIC) and the final results were tabulated.

RESULTS

Results obtained showed high variability within the same *Lactobacillus* species for the tested antibiotics (Table 1). Depending on the antimicrobial which was evaluated, the MIC results were in a broad range from 0.002 to > 32 ug/ml, independent of the preparation they originated from or the producer, but dependent on the given strain. The MIC for the same drug within one single species were often strikingly different (Figure 1).

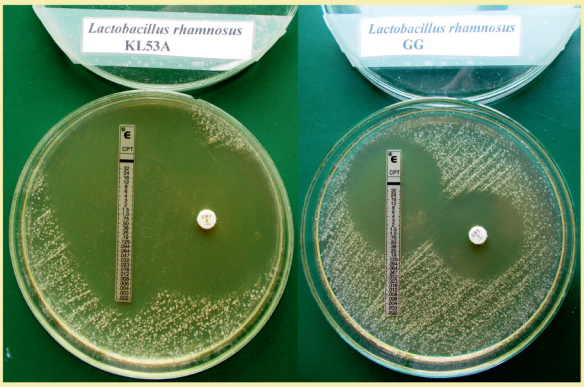

Figure 1. Significant differences regarding MIC and zones of inhibition, as shown using ceftaroline Etests and the disc diffusion test within the same *L. rhamnosus* species.

Table 1. Results of drug sensitivity testing of *Lactobacillus rhamnosus* strains using Etests. The table shows highly varied MIC values, within the same species. All species were sold in Poland as single or combined agents.

Etest	MIC (µg/ml)				
	L. rhamnosus GG	*L. rhamnosus* Pen	*L. rhamnosus* E/N	*L. rhamnosus* Oxy	*L. rhamnosus* KL53A
Ceftaroline (CPT)	0.25	0.125	0.19	0.19	< 0.002
Ceftobiprole (BPR)	0.38	> 32	0.50	0.38	0.002
Doripenem (DOR)	0.064	32	1	1	1
Daptomycin (DPC)	12	8	48	24	12
Tigecycline (TGC)	1.5	0.25	0.125	48	0.064

CONCLUSIONS

We were surprised to see that new probiotic recommendations allowed some field for extrapolation. Knowing that the devil lies in the details, in our study we wanted to try a different approach, aiming at individual strains in the same species. Despite the fact that the tested lactobacilli were strains from the same species, MIC values differed significantly for the same given drug.

We therefore propose that:
1. one should not extrapolate such important data related to drug sensitivity even within the same probiotic bacterial specie,
2. each probiotic bacterial strain should be tested for drug sensitivity since it's a strain specific characteristic.

One has to be careful in extrapolations and these results may in fact oppose the latest probiotic recommendations. We think that these results not only have some impact on the safety but also on the functionality of these strains (or more closely, the interplay between different gut bacteria and/or possible antibiotic resistance development in vivo).

References:
[1] Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, Canani RB, Flint HJ, Salminen S, Calder PC, Sanders ME. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol 2014;11:506-14.
[2] International Probiotic Conference 2010, Kosice, Slovakia, 15-17 June 2010.

Publications of poster authors may be found in: www.pubmed.com

ESCMID COLLABORATIVE CENTRE
UNIWERSYTET JAGIELLOŃSKI COLLEGIUM MEDICUM
Chair of Microbiology
Jagiellonian University
Medical College
18 Czysta Str., 31-121 Cracow
Poland

*Correspondence to:
Piotr Kochan, M.D., Ph.D.
e-mail: pkochan@cm-uj.krakow.pl
phone: +4812 633 25 67

More information about the corresponding author can be read in the first editorial on World Journal of Medical Images, Videos and Cases website: www.wjomi.com